

We claim:

1. A targeting construct comprising:
  - (a) a first polynucleotide sequence homologous to a 5-HT-2B gene;
  - 5 (b) a second polynucleotide sequence homologous to the 5-HT-2B gene; and
  - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
  - 10 (a) providing a first polynucleotide sequence homologous to a 5-HT-2B gene;
  - (b) providing a second polynucleotide sequence homologous to the 5-HT-2B ;
  - (c) providing a selectable marker; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
- 15 4. A method of producing a targeting construct, the method comprising:
  - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a 5-HT-2B gene and a second sequence homologous to a second region of a 5-HT-2B gene;
  - (b) inserting a positive selection marker in between the first and second sequences
  - 20 to form the targeting construct.
5. A cell comprising a disruption in a 5-HT-2B gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a 5-HT-2B gene.
- 25 9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in a 5-HT-2B gene, the method comprising:
  - (a) introducing the targeting construct of claim 1 into a cell;
  - (b) introducing the cell into a blastocyst;
  - 30 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a 5-HT-2B, the method comprising:

5 (a) providing a non-human transgenic animal comprising a disruption in a 5-HT-2B gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression of 5-HT-2B in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a 5-HT-2B, the method comprising:

10 (a) providing a non-human transgenic animal comprising a disruption in a 5-HT-2B gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the function of the disrupted 5-HT-2B gene in the non-human transgenic animal is modulated.

15 13. A method of identifying an agent that modulates the expression of 5-HT-2B, the method comprising:

(a) providing a cell comprising a disruption in a 5-HT-2B gene;

(b) contacting the cell with an agent; and

20 (c) determining whether expression of the 5-HT-2B is modulated.

14. A method of identifying an agent that modulates the function of a 5-HT-2B gene, the method comprising:

(a) providing a cell comprising a disruption in a 5-HT-2B gene;

(b) contacting the cell with an agent; and

25 (c) determining whether the function of the 5-HT-2B gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a 5-HT-2B gene, wherein the

30 transgenic mouse exhibits at least one of the following phenotypes: embryonic lethality, abnormal embryos, retarded development, and reabsorbed embryos.

18. The transgenic mouse of claim 17, wherein development is arrested at embryonic day 8.5.

19. The transgenic mouse of claim 17, wherein homozygous offspring are undetectable after embryonic day E8.5.

5 20. The transgenic mouse of claim 17, wherein homozygous embryos die between embryonic day 8.5 and embryonic day 9.5.

21. The transgenic mouse of claim 17, wherein the embryos are reabsorbed between embryonic day 8.5 and embryonic day 9.5.

22. A method of producing a transgenic mouse comprising a disruption in a 5-HT-2B 10 gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: embryonic lethality, abnormal embryos, retarded development, and reabsorbed embryos, the method comprising:

(a) introducing a 5-HT-2B gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

15 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a 5-HT-2B gene.

23. A transgenic mouse produced by the method of claim 22.

20 24. A cell derived from the transgenic mouse of claim 17 or claim 23.

25. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a 5-HT-2B gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a 5-HT-2B gene; and

25 (b) determining whether the agent ameliorates at least one of the following phenotypes: embryonic lethality, abnormal embryos, retarded development, and reabsorbed embryos.

26. An agonist or antagonist of a 5-HT-2B receptor.

27. Phenotypic data associated with the transgenic mouse of claim 17 or claim 23, 30 wherein the data is in a database.